Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of inducing apoptosis in a target cell, comprising:

exposing the cell to an effective amount of a differentiation inducing agent to induce differentiation of the cell; and

exposing the cell to an agent that interferes with human Notch-1 function or expression to inhibit a cell fate determining function of a human Notch-1 protein in the target cell at a time when the cell is undergoing differentiation, thereby inducing the target cell to undergo apoptosis.

2. (currently amended) The method of claim 1, wherein the target cell is a tumor cell characterized by:

(a) increased expression of the human Notch-1 protein; or

(b) increased human Notch-1 activity or expression, relative to human Notch-1 activity or expression in a same tissue type that is not neoplastic.

3.-4. (canceled)

5. (Original) The method of claim 2, wherein the tumor cell is:

(a) selected from the group consisting of cervical cancer, breast cancer, colon cancer, melanoma, seminoma, lung cancer, and hematopoietic malignancy; and

(b) is a tumor cell in a subject.

6. (Cancelled)

7. (Cancelled)

8. (previously presented) The method of claim 1, wherein the differentiation inducing agent comprises an agent selected from the group of retinoids, polar compounds, short chain fatty acids, organic acids, Vitamin D derivatives, cyclooxygenase inhibitors, arachinodate metabolism inhibitors, ceramides, diacylglycerol, cyclic nucleotide derivatives, hormones, hormone antagonists, and biologic promoters of differentiation, and derivatives thereof.

9. (Original) The method of claim 8, wherein the agent is a polar hybrid compound.

10. (Original) The method of claim 9, wherein the polar hybrid compound is hexamethylene bisacetamide (HMBA).

11. (currently amended) The method of claim 1, wherein the agent that interferes with human Notch-1 function or expression comprises an agent that interferes with expression of human Notch-1 protein in the target cell.

12. (currently amended) The method of claim 11, wherein the agent that interferes with human Notch-1 protein expression in the target cell comprises an effective amount of an antisense molecule that specifically blocks expression of human Notch-1 protein.

13. (currently amended) The method of claim 12, wherein the antisense molecule includes at least six contiguous nucleotides of a sequence that is complementary to at least a portion of an RNA transcript of a human *Notch*-1 gene, and is hybridizable to the RNA transcript.

14.-15. (canceled)

16. (previously presented) The method of claim 13, wherein the antisense molecule comprises at least six contiguous nucleotides from SEQ ID NO: 6, 8, or 11.

17. (currently amended) The method of claim 1, wherein the agent that interferes with human Notch-1 function or expression comprises an agent that antagonizes the function of the human Notch-1 protein.

18. (currently amended) The method of claim 17, wherein the agent which antagonizes the function of human Notch-1 protein comprises an antibody that specifically binds to human Notch-1, or a portion of the antibody containing a binding domain that specifically binds to human Notch-1.

19. -21. (Cancelled)

22. (Original) The method of claim 18, wherein the antibody is an antibody against the human Notch-1 EGF-repeats 11 and 12, that recognizes an extracellular epitope of Notch-1, and that stimulates target cell differentiation in the presence of an effective amount of differentiation inducing agent.

23. (previously presented) The method of claim 22, wherein the antibody is a monoclonal antibody selected from the group consisting of one or more of a) a monoclonal antibody secreted by a hybridoma designated A6 having A.T.C.C. Accession No. HB12654; b) a monoclonal antibody secreted by a hybridoma designated C11 having A.T.C.C. Accession No. HB12656; and c) a monoclonal antibody secreted by a hybridoma designated F3 having A.T.C.C. Accession No. HB12655.

24. - 29. (Cancelled)

30. (Previously presented) The method of claim 5, wherein the tumor cell is a hematopoietic malignancy or a cervical cancer in which Notch-1 expression is increased.

31. (Previously presented) The method of claim 1, wherein:

the target cell is a tumor cell in a subject, and the differentiation inducing agent is hexamethylene bisacetamide (HMBA) that is administered to the subject in a therapeutically effective amount.

32. (Previously presented) The method of claim 18, wherein exposing the cell to an effective amount of the differentiation inducing agent occurs subsequent to exposing the cell to the antibody or portion of the antibody.

33. - 71. (Cancelled)

72. (Original) The method of claim 1, further comprising treating the target cell with a therapeutically effective amount of another antineoplastic agent at a time that enhances apoptosis in the target cell.

73. (previously presented) The method of claim 72 wherein the other antineoplastic agent comprises a vinca alkaloid.

74. (previously presented) The method of claim 73 wherein the vinca alkaloid is selected from the group consisting of one or more of vinblastine, Paclitaxel and vincristine.

75. (currently amended) The method of claim 72, wherein the other antineoplastic agent is administered substantially ~~concurruently~~ concurrently with the agent administered to inhibit a cell fate determining function of a human Notch-1 protein in the target cell at a time when the cell is undergoing differentiation, which induces the target cell to undergo apoptosis.

76. - 82. (Cancelled)

83. (original) The method of claim 18, wherein the antibody specifically binds to Notch-1 protein and interferes with Notch-4 function.

84. (original) The method of claim 5, wherein the tumor cell is a breast cancer or a melanoma in which Notch-4 expression is increased.

85. (original) The method of claim 1, wherein exposing the cell to the effective amount of a differentiation inducing agent and the agent that specifically interferes with Notch function or expression comprises administration of both agents simultaneously.

86. (original) The method of claim 1, wherein exposing the target cell to the differentiation inducing agent and the agent that interferes with Notch function or expression comprises administering the agents to a subject in whom the target cell is found.

87. (new) A method of inducing apoptosis in a target cell, comprising:

exposing the cell to an effective amount of a differentiation inducing agent to induce differentiation of the cell; and

exposing the cell to an effective amount of an antisense molecule that specifically blocks expression of human Notch-1 in the target cell at a time when the cell is undergoing differentiation, wherein the antisense molecule comprises at least six contiguous nucleotides of SEQ ID NO: 6, 8, or 11, thereby inducing the target cell to undergo apoptosis.

88. (new) A method of inducing apoptosis in a target cell in vitro, comprising:

exposing the cell to an effective amount of a differentiation inducing agent to induce differentiation of the cell; and

exposing the cell to an effective amount of an antisense molecule that specifically blocks expression of human Notch-1 in the target cell at a time when the cell is undergoing differentiation, wherein the antisense molecule comprises at least six contiguous nucleotides of SEQ ID NO: 6, 8, or 11, thereby inducing the target cell to undergo apoptosis.